

**IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327
THIS DOCUMENT RELATES TO: WAVE 1 CASES	JOSEPH R. GOODWIN U.S. DISTRICT JUDGE

**DEFENDANTS' REPLY IN SUPPORT OF MOTION TO EXCLUDE
THE OPINIONS AND TESTIMONY OF DR. VLADIMIR IAKOVLEV**

Defendants Ethicon, Inc. and Johnson & Johnson (collectively, “Ethicon”) submit this Reply in Support of their Motion to Exclude the Testimony and Opinions of Dr. Vladimir Iakovlev, M.D. (“Motion”). Plaintiffs’ Response to Defendant Ethicon’s Motion to Exclude the Opinions and Testimony of Vladimir Iakovlev (“Response”) fails to address the fundamental flaws in Dr. Iakovlev’s methodology identified in Ethicon’s Motion. Instead, Plaintiffs seek to avoid the substance of Ethicon’s arguments by invoking prior orders issued when the Court did not have before it the evidence on which Ethicon now relies; mischaracterizing Ethicon’s positions; and erroneously portraying Ethicon’s arguments as reflecting a mere “difference of opinion” among the parties’ experts.

I. Dr. Iakovlev’s Failure To Test His Hypothesis That Degraded Prolene Traps Histological Stains Shows That His Degradation Opinions Are Unreliable.

A. Exponent’s Control Experiment Is Relevant and Reliable.

As explained in Ethicon’s Motion, Dr. Steven MacLean and his team of scientists (collectively, “Exponent”) conducted the test that Dr. Iakovlev has purposefully refused to

perform: a simple control experiment to assess the validity of Dr. Iakovlev's hypothesis that degraded Prolene will trap histological stains so that it can be observed as "bark" using light microscopy. *See* Mem. Law Supp. Motion to Exclude Opinions and Testimony of Dr. Vladimir Iakovlev ("Defs.' Mem.") at 6–7. Exponent subjected Prolene fibers to two oxidation methods—ultraviolet radiation ("QUV") and a chemical oxidation medium used by Plaintiffs' experts, Dr. Scott Guelcher and Dr. Russell Dunn—and then subjected the fibers to the same preparation and staining protocols used by Dr. Iakovlev. *Id.* Based on sound scientific principles, Exponent's control experiment showed that none of the Prolene fibers trapped stain, and thereby demonstrated that Dr. Iakovlev's methods are flawed and his opinions are unreliable. *Id.*

i. Exponent's control experiment shows that Dr. Iakovlev failed to follow a reliable scientific methodology.

As explained in Ethicon's Motion, Exponent's experiment shows that Dr. Iakovlev's opinion is based on a fundamentally flawed methodology. *See* Defs.' Mem. at 4–7. Dr. Iakovlev's admission that he is currently testing his hypothesis only highlights the fact that he has offered conclusions in this case based on a theory that he has not tested. *See id.* at 4–6.

Plaintiffs argue that Exponent's control experiment does not constitute a basis for excluding Dr. Iakovlev's opinions because it reflects "conflicting opinions of experts[.]" *See* Resp. at 11.¹ This is simply false. Exponent's control experiment does not merely permit Dr. MacLean to reach a different conclusion than Dr. Iakovlev, as Plaintiffs claim. Rather, the significance of Exponent's work is that it represents the control experiment that Dr. Iakovlev should have conducted *before* offering his conclusions. Put differently, even without Exponent's

¹ In response to Ethicon's challenge to Dr. Iakovlev's methods—including the control experiment conducted by Exponent which falsifies Dr. Iakovlev's hypothesis—Plaintiffs now seek to downplay the significance of Dr. Iakovlev's theory to his degradation opinions. *See, e.g.,* Resp. at 7–11. Yet, as Dr. Iakovlev's testimony, publications, and expert reports make clear, all of Dr. Iakovlev's degradation opinions flow from his alleged ability to use light microscopy to detect histological stains trapped in degraded surface of mesh fibers.

results, Dr. Iakovlev's opinions should be excluded as unreliable because he failed to test his hypothesis. The fact that Exponent's control experiment actually disproves Dr. Iakovlev's hypothesis further demonstrates the unreliability of Dr. Iakovlev's opinion.

ii. Exponent's *in vitro* control experiment is relevant.

Plaintiffs argue that Exponent's *in vitro* control experiment is irrelevant to Dr. Iakovlev's *in vivo* opinions because Dr. Robyn Prueitt—a toxicologist Ethicon did not disclose as an expert in this litigation—testified that *in vitro* testing does not replicate *in vivo* conditions. *See* Resp. at 11–12.

As an initial matter, it is clear from the very same page of Dr. Prueitt's testimony to which Plaintiffs cite that her testimony specifically pertained to a well-known toxicological concept. *See* Resp. Ex. D, Prueitt 10/22/15 Dep. Tr. 89:1–90:4. Specifically, Dr. Prueitt explained that *in vitro* testing is primarily useful as a screening mechanism, because if highly concentrated doses of the substance at issue applied directly to cells do not cause toxicological effects, no such effects would be expected *in vivo*. *See id.* Conversely, *in vitro* testing alone is insufficient to make causal conclusions about *in vivo* toxicity, because the tests directly expose living cells to much greater concentrations of potential toxins than would ever be present *in vivo*. *See id.*; *see also id.* at 134:11–135:4. As Dr. Prueitt's testimony clearly dealt with questions of toxicology, Plaintiffs' argument is without merit.

In addition, Plaintiffs misunderstand the meaning of the term *in vitro*. *In vitro* testing refers to the study of cells and other biological materials outside of their normal environment. *See, e.g., Bourne ex rel. Bourne v. E.I. DuPont de Nemours & Co., Inc.*, 189 F. Supp. 2d 482, 489 n.14 (S.D.W. Va. 2002) (“*In vitro* tests involve the exposure of isolated cell systems to a particular substance under controlled laboratory conditions within a test tube or petri dish.”). Dr.

MacLean has conducted no such testing. Rather, he conducted an *ex vivo* control experiment that focused on the question of whether intentionally oxidized Prolene fibers can trap histological stains. *See* Mot. Ex. I, Expert Report of Dr. Steven MacLean (“MacLean Report”) at 54–68. In other words, the inquiry is focused on the effect of histological stains to the fiber itself, not the effect of the fiber on cells in the human body. Plaintiffs’ argument is simply inapposite.

Moreover, Exponent used chemical- and QUV-oxidation methods that far exceed the oxidative capacity of anything found in a woman’s pelvic floor. *See id.* at 54–56. As such, the fact that the Prolene fibers did not trap stain indicates that Prolene fibers would not do so after exposure to *in vivo* conditions. Plaintiffs’ attempt to exclude Exponent’s testing based on basic principles of cytotoxicology is not only inapposite, but it actually contradicts their argument.

iii. Plaintiffs ignore the fact that Exponent’s control experiment analyzed Prolene fibers subjected to two separate oxidation methods, and confirmed cracking in QUV-treated Prolene fibers.

Plaintiffs argue that Exponent’s control experiment is unreliable because it allegedly did not actually analyze oxidized Prolene. *See* Resp. at 12–13. Plaintiffs’ claim that Exponent erred by following a protocol used by Plaintiffs’ own experts—Drs. Scott Guelcher and Russell Dunn—which called for exposing mesh samples to a chemical oxidative medium for five weeks. *See id.* Plaintiffs assert that Exponent should have followed Dr. Iakovlev’s approach, which involves exposing the mesh to the chemical oxidative medium for up to 18 months. *Id.* Significantly, Dr. Iakovlev has refused to follow his own protocol—he still has not tested his theory even though it has now been more than 18 months. Mot. Ex. B, Iakovlev 3/21/16 (*Stubblefield*) Dep. Tr. 64–65.

Plaintiffs ignore the fact that Exponent subjected Prolene samples to two oxidation methods. *See* Mot. Ex. I, MacLean Report at 54–56.² In addition to following the protocol used by Drs. Guelcher and Dunn that Plaintiffs now dismiss as invalid, Exponent ensured that they would have at least some oxidized Prolene fibers on which to conduct their experiment by subjecting one batch of Prolene samples to ultraviolet radiation (“QUV”). *Id.* The QUV treatment is widely recognized in scientific literature to oxidize polypropylene, including Prolene. *Id.*; *see also* Reply Ex. KK, Benight 10/13/15 Dep. Tr. 214:6–13 (explaining that they conducted a QUV treatment “because that’s covered in over hundreds of literature articles . . . including intentionally oxidizing polymer samples”).

Exponent conducted SEM and FTIR on the samples, and found that while the QUV-treated fibers exhibited clear evidence of surface cracking, the chemically oxidized samples did not. *See* Mot. Ex. I, MacLean Report at 56. With respect to the QUV-treated fibers subjected to Dr. Iakovlev’s staining protocol, Exponent confirmed surface cracking using SEM. *See, e.g., id.* at 56 (fig. 10), 57 (fig. 12), 62 (fig. 19).

Notably, Plaintiffs do not even mention the QUV-treated samples used in the control experiment. *See* Resp. at 11–13.

Plaintiffs misunderstand the results of Exponent’s control experiment. Neither Ethicon nor Exponent ever claimed that the Prolene fibers exposed to the chemical oxidation medium showed surface cracking. In fact, quite the opposite. *See, e.g.,* Mot. Ex. I, MacLean Report at 56. By focusing solely on the chemically treated fibers, Plaintiffs ignore the fact that the QUV-treated fibers were confirmed to have oxidized and cracked, but still did not trap histologic stains as Dr. Iakovlev claims.

² As explained in Ethicon’s Response in Opposition to Plaintiffs’ Motion and Memorandum to Exclude the Opinions and Testimony of Defendant Ethicon, Inc.’s Expert Steven MacLean, Ph.D., P.E., Plaintiffs arguments regarding Dr. MacLean’s opinions and control experiment are without merit.

Plaintiffs' arguments that Exponent's control experiment was unreliable are meritless, and should be rejected by this Court.

B. Dr. Iakovlev's Testimony Undercuts Plaintiffs' Efforts to Distance Themselves from Dr. Iakovlev's Testing.

Although Plaintiffs argue that Dr. Iakovlev's current testing does not address whether the allegedly oxidized and degraded outer layer of a mesh fiber traps histological stain (Resp. at 8–11), Dr. Iakovlev's deposition testimony belies their claim. Indeed, on the very same page of Dr. Iakovlev's deposition transcript to which Plaintiffs cite, Dr. Iakovlev acknowledges that this is the precise purpose of his testing:

Q. And as a part of your experiment do you then intend to see whether—if you are able to oxidize polypropylene, according to your visual observation by light microscopy, will you then see whether the oxidized polypropylene holds stain?

A. Yes, that's the way to see it. This just becomes porous and after absorbs stain.

See Mot. Ex. E, Iakovlev 9/11/15 Dep. at 45:9–16 (emphasis added); *see also id.* at 44:12–26 (agreeing that the “reason why you're doing this test is to determine whether, first, after 18 months this polypropylene will oxidize due to exposure to this chemical mixture” using light microscopy).

But assuming Plaintiffs are correct and Dr. Iakovlev is not performing these tests to verify his hypothesis, the fact that he does not recognize the scientific necessity of conducting a control experiment to determine whether his theory is even possible only demonstrates that he does not understand the scientific method.

C. No Scientific Or Medical Literature Supports Dr. Iakovlev's “Bark” Theory

Plaintiffs claim that Ethicon's argument that “there is no scientific or medical evidence to support Dr. Iakovlev's opinions concerning degradation ‘bark’ from explanted mesh *in vivo* is simply wrong.” *See* Resp. at 13. Remarkably, in the very next paragraph, Plaintiffs apparently

concede that no scientific or medical literature supports Dr. Iakovlev's bark theories by asserting that the lack of such support is immaterial. *Id.*

Recognizing that no scientific literature supports Dr. Iakovlev's theory that degraded Prolene can be detected using histological stains and light microscopy, Plaintiffs change the inquiry by pointing to papers and internal Ethicon studies which, according to Plaintiffs, support Dr. Iakovlev's bark theories. *See* Resp. at 14–17. But while some of these materials contain sound bites to which Plaintiffs can point, a closer review of these studies reveals that they fail to support Plaintiffs arguments.

Only one of the studies employed methods similar to those used by Dr. Iakovlev, and that study is subject to the same criticisms as Dr. Iakovlev's methodology. Specifically, the researchers in the 1984 "Ethicon Research Foundation" study conducted their test without running a control experiment to validate the underlying hypothesis that degraded Prolene would hold stain. *See* Reply Ex. LL, ETH.MESH.15955462. Dr. MacLean has performed that experiment, and invalidated this hypothesis. *See* Defs.' Mem. at 6–7. Plaintiffs ask this Court to hold Ethicon's state of scientific knowledge to testing that took place 32 years ago without regard for advances in scientific methods and understanding, including the fact that the hypothesis underlying the testing has now been disproven. The Court should reject Plaintiffs' invitation to ignore the scientific method, which necessarily requires "subjecting testable hypotheses to the crucible of experiment in an effort to disprove them." *United States v. Bynum*, 3 F.3d 769, 773 (4th Cir. 1993).

Ultimately, Plaintiffs argument that the Court's focus should be on Dr. Iakovlev's methods disregards the fact that the absence of scientific or medical literature supporting his opinions, coupled with his failure to test his hypothesis, speaks *directly* to his poor methodology.

See Defs.’ Mem. at 6–7. Ethicon’s argument is not, as Plaintiffs claim, merely that Dr. Iakovlev’s conclusions have not been published or are simply incorrect. *See* Resp. at 13–14. Rather, as discussed in Ethicon’s Motion, Dr. Iakovlev’s opinions are not based on a reliable scientific methodology because he has not tested the basis for his degradation opinions, and no scientific or medical literature supports Dr. Iakovlev’s opinions regarding degradation bark. *See* Defs.’ Mem. at 4–9 (explaining Dr. Iakovlev’s own papers are the only publications that support his theories, and even his own papers call his theories into question).

D. Dr. Iakovlev’s Degradation Theories Are Not Supported By Scientific Literature.

Recognizing that Dr. Iakovlev’s bark theory is unreliable, Plaintiffs claim that his opinions “that Ethicon’s mesh products degrade *in vivo* are based on the well-documented medical and scientific literature that he cites in his report, as well as the Ethicon documents that confirm the existence of degradation.” Resp. at 7. Indeed, Plaintiffs claim that Dr. Iakovlev’s degradation opinions are supported by “dozens of published scientific articles and numerous Ethicon documents in his 30-page reliance list,” and that he “details his degradation opinions, supporting each such opinion with a wealth of published literature as well as internal Ethicon degradation testing and sworn testimony.” *Id.* at 5.

Plaintiffs’ suggestion that the 500 scientific articles and Ethicon documents in Dr. Iakovlev’s reliance list support his degradation opinions is false. In addition, although Plaintiffs repeatedly claim that Dr. Iakovlev’s opinions are supported by scientific and medical literature, they do not point the Court to a single document supporting his degradation opinions. *See id.* at 5–6, 13–17.

More importantly, as explained in Ethicon’s Motion, Dr. Iakovlev’s own publications demonstrate that the opinions he seeks to offer to a reasonable degree of scientific certainty in

Court are not supported by scientific literature other than his own writings, one of which even concedes that “the question of whether polypropylene degrades *in vivo* has not been fully resolved, despite decades of use.” *See* Defs.’ Mem. at 8–9, 10; *see also* Mot. Ex. O, Blaivas, et al., *Safety Considerations for Synthetic Sling Surgery*, *Nature Rev. Urology*, at 17 (2015).

Thus, Dr. Iakovlev’s own writings belie Plaintiffs suggestion that his opinions are consistent with the body of scientific literature. Accordingly, the Court should exclude Dr. Iakovlev’s opinions regarding degradation in this case.

E. Dr. Iakovlev’s Own Writings Show that His Opinion That Degradation Causes Complications Is Unreliable.

Plaintiffs did not directly respond to Ethicon’s challenge to Dr. Iakovlev’s opinions regarding the complications allegedly caused by degradation, which is based on Dr. Iakovlev’s own publications. *See* Defs.’ Mem. at 9–11. Instead, Plaintiffs claim that he is qualified by training to opine on these issues, and point to a previous order issued by this Court that Ethicon respectfully submits is distinguishable from this case. *See* Resp. at 17–19. Specifically, Plaintiffs’ argument fails because the evidence on which Ethicon bases its arguments in this case was not before the Court when it issued its decision in *Edwards*.

In arguing that Dr. Iakovlev’s degradation opinions are based on the “weight of [the] evidence,” (Resp. at 19), Plaintiffs ignore the fact that the evidence contradicting Dr. Iakovlev’s opinions includes Dr. Iakovlev’s own publications (Defs.’ Mem. at 9–11). Grasping at straws, Plaintiffs assert that Ethicon’s arguments are based on “selective quotes” and “out of context citations” from Dr. Iakovlev’s writings. Resp. at 19. Notably, Plaintiffs do not actually dispute that Dr. Iakovlev’s out-of-court writings state that the scientific literature has not shown that degradation causes complications in patients. *See* Resp. at 17–19.

Accordingly, the Court should exclude Dr. Iakovlev's opinions that the alleged degradation of Prolene causes complications.

II. Dr. Iakovlev's Opinions Regarding Complications Are Unreliable.

A. Dr. Iakovlev's Failure to Compare His Pathological Findings to an Asymptomatic Control Shows that His Opinions Are Unreliable.

Plaintiffs misunderstand Ethicon's arguments regarding Dr. Iakovlev's failure to compare his pathological findings to an asymptomatic control because they claim that Dr. Iakovlev testified that certain features of the slides he reviewed contained abnormalities. *See* Resp. at 20–21.

Ethicon's Motion explains that Dr. Iakovlev's opinions are unreliable because he did not compare the slides in which he allegedly found evidence of pain to explants from patients who did not complain of pain. *See* Defs.' Mem. at 11–12. Contrary to Plaintiffs' misleading assertion that such comparisons would be unethical and amoral, (Resp. at 21 n.33), Dr. Iakovlev could have used a proper control by looking at meshes removed from patients for reasons other than pain. Indeed, this is precisely what the scientists at the Cleveland Clinic did in the Hill study. *See* Defs.' Mem. at 11–14.

A scientist cannot dispense with the requirements of the scientific method simply because compliance is inconvenient for him. And a conclusion offered in the absence of a proper control is not scientifically valid simply because a control was not used when the test was run. Here, even if the Hill study did not exist or it was not possible for Dr. Iakovlev to locate explants from patients who did not complain of pain, the scientific method dictates that Dr. Iakovlev cannot offer a conclusion because he cannot account for the potential that patients with no pain would have the exact same pathological presentation.

In addition, none of the testimony to which Plaintiffs cites shows that Dr. Iakovlev used a control in his analysis. *See* Resp. at 20 (citing Resp. Ex. B, Iakovlev 9/14/15 Dep. Tr. 99:8–10; 99:14–15; 117:8–13; 118:4–20; 121:12–16; 127:8–11). At most, the testimony shows that Dr. Iakovlev compared one of his pathological findings to normal tissue *within the same slide*. *See, e.g.,* Resp. Ex. B, Iakovlev 9/14/15 Dep. Tr. 118:4–20. But, by definition, a control cannot come from the same specimen under examination.

Ultimately, Plaintiffs misapprehend the significance of using controls in pathological analysis. As Ethicon explained, without comparing the histological slide of a patient who complained of pain to the slide from a patient who did not complain of pain, the pathologist’s findings cannot be said to identify the cause of the patient’s pain. *See* Defs.’ Mem. at 11 (citing Mot. Ex. P, Felix Report at 11–12, Mot. Ex. S, Longacre Report at 4–5; Mot. Ex. T, McLendon Report at ¶ 6; Mot. Ex. U, Vogel Report at 14). Despite Plaintiffs’ suggestion to the contrary (Resp. at 20–21), Dr. Iakovlev’s comparison of his pathological findings to normal tissue within the same slide does not constitute a control, since he cannot rule out the fact that patients not suffering from pain may have the same pathological presentation based on this comparison.

Because Dr. Iakovlev’s opinions that mesh causes pain in patients are nothing but speculation, the Court should exclude them from trial.

B. Dr. Iakovlev’s Failure To Account For The Findings Reported In Scientific Literature Shows That His Opinions Are Unreliable.

Plaintiffs assert that Dr. Iakovlev did not ignore relevant scientific literature because he “relies on over 600 scientific articles and Ethicon documents—including the literature that he himself has authored.” Resp. at 21. As discussed in Ethicon’s Motion, however, Dr. Iakovlev’s own review article explained that “only a few published studies exist in which investigators actually examined histological changes in mesh explants that had been removed from humans.”

Defs.’ Mem. at 12 (quoting Mot. Ex. O, Blaivas, *et al.*, *Safety Considerations for Synthetic Sling Surgery*, *Nature Rev. Urology*, at 15 (2015)). Thus, Dr. Iakovlev’s own writings dispel Plaintiffs’ suggestion that his opinions regarding complications are based on the 600 documents included in his reliance list.

Plaintiffs also fail to understand Ethicon’s arguments with respect to the Hill study. In addition to disregarding Hill’s teachings regarding the use of a control, Plaintiffs’ argue that the Hill study is irrelevant because it “addressed the correlation between chronic (lymphocytic) inflammation and pain, NOT the correlation between foreign body type inflammation and pain.” Resp. at 21 n.34. Even a superficial reading of the study demonstrates that Plaintiffs’ assertion is false. *See* Mot. Ex. C, Hill at 594 (“Approximately 90% of the pathological specimens in our study were found to have evidence of a giant cell reaction,” which is “is referred to as the ‘foreign body reaction.’”). Indeed, the Hill study expressly states that the “presence or absence of giant cell reaction was also recorded” as part of the study’s methodology. *Id.* at 592.

Moreover, Ethicon’s argument is not merely that the Hill study “was not included on [Dr. Iakovlev’s] extensive reliance list” as Plaintiffs suggest (Resp. at 21), but that Dr. Iakovlev failed to consider its findings that are directly relevant to his opinions. *See* Defs.’ Mem. at 12–14. Given that Dr. Iakovlev testified that his opinions were based on his review of the relevant scientific literature, Dr. Iakovlev’s failure to locate the single most relevant study to his opinions—in what his own writings suggest is a limited field of literature—shows that he followed a poor methodology in conducting his literature review.

Finally, Plaintiffs erroneously allege that Ethicon “blatantly misrepresented to this Court” the studies on which Dr. Iakovlev relied.³ *See* Resp. at 21. Ethicon’s Motion clearly states that Dr. Iakovlev ignored the findings of relevant scientific literature. *See* Defs.’ Mem. at 12 (“Dr. Iakovlev ignores relevant scientific literature” and “Dr. Iakovlev failed to account for scientific literature relevant to his opinions.”), 13 (“Dr. Iakovlev’s failure to account for the Hill study is not an isolated incident.”). Ethicon explained that Dr. Iakovlev made no effort to reconcile his opinions in this case with the findings reported in the scientific literature, including his own work. *Id.* at 13 (citing Mot. Ex. T, McClendon Expert Report at ¶¶ 8, 10; Mot. Ex. P, Felix Expert Report at 16). Indeed, Plaintiffs’ emphasis on Dr. Iakovlev’s authorship of one of the studies to which Ethicon points (Resp. at 21) highlights their failure to grasp the significance of the disparity between Dr. Iakovlev’s opinions in litigation and his out-of-court writings. *See Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999). Thus, it cannot be said that Dr. Iakovlev accounted for these studies that contradict his opinions.

Despite Plaintiffs’ assertion to the contrary (Resp. at 21–22), the fact that Dr. Iakovlev wrote a paper or included a study on his reliance list does not establish that he properly accounted for its findings in his opinions. This is particularly evident in this litigation where he has made no effort in his Report or testimony to address the different findings reported in the scientific literature.

III. Dr. Iakovlev’s Failure To Follow A Proper Scientific Methodology Shows That His Opinion That TVT Causes Pain Is Unreliable.

In response to Ethicon’s arguments that Dr. Iakovlev’s opinions regarding pain are unreliable and methodologically unsound, (Defs.’ Mem. at 16–18), Plaintiffs do not actually

³ Throughout their Response, Plaintiffs repeatedly assert that Ethicon made misrepresentations to the Court. *See* Resp. at 7, 12, 14, 16, 17, 19. Plaintiffs’ allegations regarding Ethicon’s candor toward this Court are highly inappropriate, particularly where Plaintiffs failed to substantiate any of their claims.

dispute the substance of Ethicon's position (Resp. at 22). Instead, Plaintiffs point to a distinguishable prior ruling, and claim that the results in this case should be no different. *See* Resp. at 22 (quoting *Edwards v. Ethicon, Inc.*, No. 2:12-cv-09972, 2014 WL 3361923, at *69–70 (S.D.W. Va. July 8, 2014)). Yet, Plaintiffs ignore the fact that the evidence on which Ethicon bases its arguments in this case was not before the Court when it issued its order in *Edwards*.

In addition, Plaintiffs claim that Ethicon's arguments based on the expert reports submitted by Ethicon's neuropathologists amount to nothing more than "differing conclusions" from the parties' experts. *See id.* Plaintiffs fail to understand that Ethicon did not merely challenge Dr. Iakovlev's conclusions, but his methodology. *See* Defs.' Mem. at 16–18.

Based on the opinions and testimony of neuropathologists—who, unlike Dr. Iakovlev, have specialized education, training, and experience in the identification of nerves and nerve components, as well as the diagnosis of nerve-related complications—Ethicon explained that Dr. Iakovlev's opinions are not based on sound scientific methods or medical facts. *See id.*

In failing to address any of Ethicon's specific arguments, Plaintiffs offer no explanation as to how the numerous methodological flaws outlined in the Motion could be construed as mere differences of opinion. Moreover, even a cursory review of the expert reports submitted by Drs. Vogel and McClendon demonstrates that their opinions go well beyond "differing conclusions."

Accordingly, the Court should reject Plaintiffs' arguments, and preclude Dr. Iakovlev from opining that TVT causes pain in women.

IV. Dr. Iakovlev's Theories that All Erosions Are Associated with Infection Is Unsupported by Scientific Literature and Relies on Unsound Logic.

In support of Dr. Iakovlev's theory that all erosions are associated with infection, Plaintiffs do not cite to any peer-reviewed medical literature supporting such a position. Instead, Plaintiffs cite to Dr. Bernd Klosterhalfen's report from the TVM study. Resp. at 23–24. Dr.

Klosterhalfen's report noted: "Infection is commonly observed following erosion in the vaginal mucosa. Primary infection without mucosal erosion is seldom found." Resp. Ex. R.

Even if Dr. Klosterhalfen's non-peer-reviewed observations from a single study would be the type of material a pathologist would normally rely upon in forming their opinions, this report does not support Dr. Iakovlev's infection opinions. At most, Dr. Klosterhalfen's show a potential correlation between infection and erosion; it is axiomatic that correlation alone is not causation. Dr. Iakovlev cannot reliably extend Dr. Klosterhalfen's observation of a "commonly observed" association between infection and erosion into the categorical rule that erosion always equals infection.

Further, Dr. Klosterhalfen's observation only suggests that an infected mesh will likely be eroded. In other words, Dr. Klosterhalfen's observations might support the following proposition: If a patient's wound is infected, then the patient's mesh is (likely) eroded. Dr. Iakovlev, on the other hand, opines that the presence of erosion conclusively proves infection. *See* Mot. Ex. AA, Iakovlev 3/13/16 (*McBrayer*) Dep. Tr. 14:2–6; Mot. Ex. BB, Iakovlev 3/4/16 (*Funderburke*) Dep. Tr. 25:12 (same); *see also* Mot. Ex. BB, Iakovlev 3/4/16 (*Funderburke*) Dep. Tr. 24:17–25:21 (explaining that a "diagnosis was made [of] vaginal erosion, which comes together with infection"). In other words, Dr. Iakovlev's opinion is that because a patient's mesh has eroded, the patient, by definition, had a wound infection. This is a logical fallacy⁴ that cannot establish any support for Dr. Iakovlev's infection opinions.

Because there is no reliable basis for Dr. Iakovlev's infection opinions, the Court should exclude them.

⁴ Specifically, "[t]his is the fallacy of affirming the consequent introduced in the elementary study of logic, often in the form: 1) if there were an invisible cat in the room I couldn't see it; 2) I can't see any cats; 3) therefore there is an invisible cat in the room." *Toussant v. Good*, No. 3:05-cv-443-KRG-KAP, 2008 WL 2994768, at *2 n.1 (W.D. Pa. 2008).

V. Dr. Iakovlev's Opinions Regarding Mesh "Compartments" and Mesh Deformation Are Unreliable.

Plaintiffs improperly claim that Ethicon "misrepresents the record to the Court" when it asserts that Dr. Iakovlev's mesh deformation opinions are unsupported and "novel." *See Resp. at 23.*

As an initial matter, Plaintiffs conflate two related, but distinct arguments made by Ethicon. As Ethicon's Motion makes clear, Ethicon first explained that Dr. Iakovlev's "compartment" theory was "novel" and lacking in support from the scientific and medical literature. *See Defs.' Mem. at 20.* This is because Dr. Iakovlev's Report does not cite any scientific literature to support his theory that interactions between mesh and scar tissue forms compartments *in vivo*. *See Mot. Ex. D, Iakovlev Report at 12, 14–19.*

Turning to Dr. Iakovlev's opinions on mesh curling and deformation, Ethicon explained that Dr. Iakovlev failed to follow the well-established methodology used by pathologists for determining how a specimen appeared *in vivo*. *Defs.' Mem. at 20–21.* Ethicon also showed that Dr. Iakovlev admitted that he cannot determine whether any alleged deformation he observes occurred during the implant surgery. *Id. at 21.* Finally, Ethicon demonstrated that Dr. Iakovlev did not properly consider the effects of the specialized tissue in the pelvic floor on the mesh during and after the explant surgery. *Id.*

Plaintiffs did not respond to any of Ethicon's arguments. *See Resp. at 23.* Rather, they once again seek to re-cast Ethicon's methodological challenge, claiming that it is a mere difference of opinion among the parties' experts. But Plaintiffs' responses simply do not apply to the arguments advanced in Ethicon's Motion, and should be rejected by this Court.

VI. Dr. Iakovlev's Opinions Based On His Mesh Samples Are Unreliable.

Plaintiffs respond to Ethicon's argument that Dr. Iakovlev's opinions based on mesh not at issue in this case are unreliable by asserting that Dr. Iakovlev's meshes came from Plaintiffs in this case, peer-reviewed literature, or Dr. Iakovlev's own prior reports. *See* Resp. at 24–25.

As an initial matter, Plaintiffs overlook this Court's prior rulings on this precise issue, in which the Court has precluded Dr. Iakovlev from testifying based on the meshes in his pool. *See, e.g., Carroll v. Bos. Sci. Corp.*, No. 2:13-cv-11601, at 23–24 (S.D.W. Va. May 6, 2016) [ECF No. 105] (excluding Dr. Iakovlev's general causation opinions based on his mesh pool); *Bethune v. Bos. Sci. Corp.*, No. 2:13-cv-06199, at 23–24 (S.D. W. Va. May 6, 2016) [ECF No. 93] (same).

In addition, Plaintiffs do not dispute the fact that Dr. Iakovlev has admitted that many of those meshes came from plaintiffs' counsel in mesh litigation. *See* Defs.' Mem. at 22. Nor do they address the fact that Dr. Iakovlev testified that he might not be able to trace some of his meshes back to a specific patient. *See id.* at 22. Thus, Plaintiffs' claim that Ethicon engaged in nothing but a "memory test at the deposition" rings hollow. As explained in Ethicon's Motion, Dr. Iakovlev's inability to determine the origins of the mesh specimens used in his Report demonstrates that he used a poor scientific methodology in developing his opinions. *Id.* at 22–23.

For the reasons identified in this Court's prior rulings, as well as those identified in Ethicon's Motion and this Reply, the Court should exclude Dr. Iakovlev's opinions based on meshes not at issue in this litigation.

VII. Conclusion

For the reasons set forth above and in Defendants' Motion, the Court should exclude the opinions and testimony of Dr. Vladimir Iakovlev.

Respectfully submitted,

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**IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327
THIS DOCUMENT RELATES TO: WAVE 1 CASES	JOSEPH R. GOODWIN U.S. DISTRICT JUDGE

CERTIFICATE OF SERVICE

I hereby certify that on May 16, 2016, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to CM/ECF participants registered to receive service in this MDL.

/s/ Philip J. Combs

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